

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
8 July 2004 (08.07.2004)

PCT

(10) International Publication Number
WO 2004/057025 A3

(51) International Patent Classification⁷: **C12Q 1/68**

(21) International Application Number:
PCT/EP2003/014813

(22) International Filing Date:
22 December 2003 (22.12.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
PCT/EP02/14877
20 December 2002 (20.12.2002) EP

(71) Applicant (for all designated States except US): **BIODETECTION SYSTEMS B.V.** [NL/NL]; Badhuisweg 3, NL-1031 CM Amsterdam (NL).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **VAN DER BURG, Bart** [NL/NL]; Tuurdijk 17, NL-3997 MS 't Goy (NL). **SONNEVELD, Edwin** [NL/NL]; Etta Palmstraat 34, NL-2135 LE Hoofddorp (NL). **BROUWER, Abraham** [NL/NL]; Gang 14, NL-2242 KD Wassenaar (NL).

(74) Agent: **VERNOUT, Robert**; Arnold & Siedsma, Sweelinckplein 1, NL-2517 GK Den Haag (NL).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

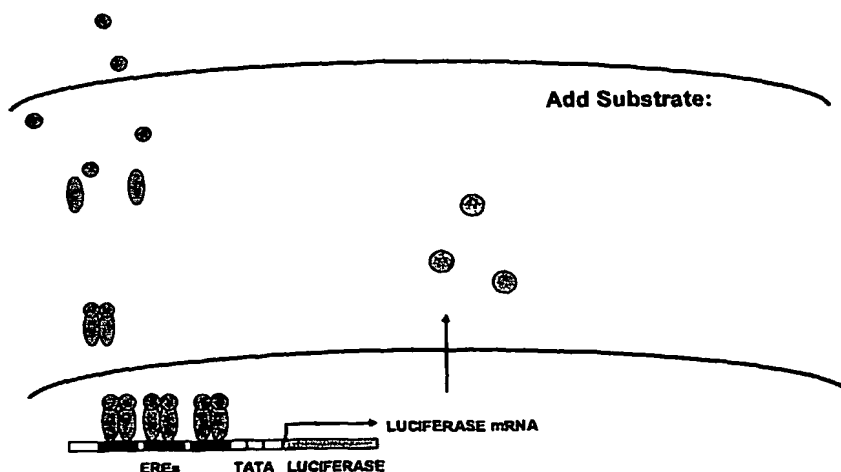
Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:
5 August 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHOD FOR DETERMINING THE PRESENCE OF ONE OR MORE LIGANDS IN A SAMPLE



(57) Abstract: The present invention relates to a method for determining the presence of one or more specific ligands in a sample, said method comprising; a) contacting the sample with an array of cell lines, each cell line comprising a reporter gene construct responding to a cellular pathway which is induced by a different specific ligand; b) measuring the activity of the reporter gene in the individual cell lines; c) comparing the measured activity in the individual cell lines; and d) determining the presence of the ligands in the sample based on said comparison.

WO 2004/057025 A3

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 03/14813

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C12Q1/68		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) IPC 7 C12Q		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, BIOSIS, EMBASE, WPI Data		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X, Y	QUAEDACKERS M E ET AL: "4-hydroxytamoxifen trans-represses nuclear factor-kappa B activity in human osteoblastic U2-OS cells through estrogen receptor (ER)alpha, and not through ER beta." ENDOCRINOLOGY. MAR 2001, vol. 142, no. 3, March 2001 (2001-03), pages 1156-1166, XP0001180339 ISSN: 0013-7227 abstract page 1157, right-hand column - page 1158, left-hand column page 1160, left-hand column; figures 1-5 <div style="text-align: center;">----- -/--</div>	1-17
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C. <input checked="" type="checkbox"/> Patent family members are listed in annex.		
* Special categories of cited documents : <div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <p>*A* document defining the general state of the art which is not considered to be of particular relevance</p> <p>*E* earlier document but published on or after the international filing date</p> <p>*L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>*O* document referring to an oral disclosure, use, exhibition or other means</p> <p>*P* document published prior to the international filing date but later than the priority date claimed</p> </div> <div style="width: 45%;"> <p>*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</p> <p>*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art</p> <p>*G* document member of the same patent family</p> </div> </div>		
Date of the actual completion of the international search	Date of mailing of the international search report	
13 April 2004	14/06/2004	
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016		Authorized officer Leber, T

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 03/14813

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,Y	<p>GRAD J M ET AL: "The androgen receptor (AR) amino-terminus imposes androgen-specific regulation of AR gene expression via an exonic enhancer." ENDOCRINOLOGY. MAR 2001, vol. 142, no. 3, March 2001 (2001-03), pages 1107-1116, XP0001180513 ISSN: 0013-7227 page 1108, right-hand column - left-hand column figures 4,5</p>	1-17
X,Y	<p>ROGATSKY I ET AL: "Factor recruitment and TIF2/GRIPI corepressor activity at a collagenase-3 response element that mediates regulation by phorbol esters and hormones." THE EMBO JOURNAL. 1 NOV 2001, vol. 20, no. 21, 1 November 2001 (2001-11-01), pages 6071-6083, XP0001180511 ISSN: 0261-4189 page 6080, left-hand column - page 6081, left-hand column figures 1,2,4,5</p>	1-17
Y	<p>BEATO M: "GENE REGULATION BY STEROID HORMONES" CELL, CELL PRESS, CAMBRIDGE, NA, US, vol. 56, no. 3, 10 February 1989 (1989-02-10), pages 335-344, XP000051659 ISSN: 0092-8674 page 336; figure 2</p>	9,13
Y	<p>LEGLER J ET AL: "Development of a stably transfected estrogen receptor-mediated luciferase reporter gene assay in the human T47D breast cancer cell line." TOXICOLOGICAL SCIENCES : AN OFFICIAL JOURNAL OF THE SOCIETY OF TOXICOLOGY. MAR 1999, vol. 48, no. 1, March 1999 (1999-03), pages 55-66, XP0009028295 ISSN: 1096-6080 page 64, left-hand column</p>	11,12
Y	<p>US 2002/137019 A1 (MARKUS STEVEN ET AL) 26 September 2002 (2002-09-26) paragraphs '0163! - '0164!; figure 12</p>	11,12
A	<p>US 6 103 479 A (TAYLOR D LANSING) 15 August 2000 (2000-08-15)</p>	
	-/--	

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 03/14813

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>WILSON VICKIE S ET AL: "A novel cell line, MDA-kb2, that stably expresses an androgen- and glucocorticoid-responsive reporter for the detection of hormone receptor agonists and antagonists."</p> <p>TOXICOLOGICAL SCIENCES : AN OFFICIAL JOURNAL OF THE SOCIETY OF TOXICOLOGY. MAR 2002, vol. 66, no. 1, March 2002 (2002-03), pages 69-81, XP0009028294 ISSN: 1096-6080</p> <p>-----</p>	

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 03/14813

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 2002137019	A1	26-09-2002	AU 4940101 A WO 0172332 A1	08-10-2001 04-10-2001
US 6103479	A	15-08-2000	US 5989835 A AU 730100 B2 AU 6667898 A CA 2282658 A1 CA 2410688 A1 EP 0983498 A1 JP 2000509827 T JP 2002355090 A WO 9838490 A1 US 6548263 B1 US 6671624 B1 US 2003096322 A1 US 6620591 B1 US 2004009539 A1 US 6416959 B1 US 6573039 B1 US 2004063162 A1 AU 734704 B2 AU 3297197 A CA 2257287 A1 EP 0912892 A1 JP 2000512009 T WO 9745730 A1	23-11-1999 22-02-2001 18-09-1998 03-09-1998 03-09-1998 08-03-2000 02-08-2000 10-12-2002 03-09-1998 15-04-2003 30-12-2003 22-05-2003 16-09-2003 15-01-2004 09-07-2002 03-06-2003 01-04-2004 21-06-2001 05-01-1998 04-12-1997 06-05-1999 12-09-2000 04-12-1997